

FIGURE 1A-1

GCG CGC CGG CCT GAG AGC CCT GTG GAC AAC CTC ATC TCG TGC TTC AGG GCC AGG GTG AAA ATG
 CCT GCT TCT CTA AGT GGG CAG CGG ACA GCG GCA CGC ACA TTT CAC CTG TCC CGC AGA CAA
 CAG CAC CAT CTG CTT GGG AGA ACC CTC TCC CTT CTC TGA GAA AGA AAG ATG TCG AAT GGG
 TAT TCC ACA GAC GAG AAT TTC CGC TAT CTC ATC TCG TGC TTC AGG GCC AGG GTG AAA ATG
 Y S T D E N F R Y L I S C F R A R V K M
 TAC ATC CAG GTG GAG CCT GTG CTG GAC TAC CTG ACC TTT CTG CCT GCA GAG GTG AAG GAG
 Y I Q V E P V L D Y L T F L P A E V K E
 CAG ATT CAG AGG ACA GTC GCC ACC TCC GGG AAC ATG CAG GCA GTT GAA CTG CTG CTG AGC
 Q I Q R T V A T S G N M Q A V E L L L S
 ACC TTG GAG AAG GGA GTC TGG CAC CTT GGT TGG ACT CGG GAA TTC GTG GAG GCC CTC CGG
 T L E K G V W H L G W T R E F V E A L R
 AGA ACC GGC AGC CCT CTG GCC GGC TAC ATG AAC CCT GAG CTC ACG GAC TTG CCC TCT
 R T G S P L A A R Y M N P E L T D L P S
 CCA TCG TTT GAG AAC GCT CAT GAT GAA TAT CTC CAA CTG AAC CTC CTT CAG CCC ACT
 P S F E N A H D E Y L Q L N L L Q P T
 CTG GTG GAC AAG CTT CTA GTT AGA GAC GTC TTG GAT AAG TGC ATG GAG GAG GAA CTG TTG
 L V D K L L V R D V L L D K C M E E L L
 ACA ATT GAA GAC AGA AAC CGG ATT GCT GCT GCA GAA AAC AAT GGA AAT GAA TCA GGT GTA
 T I E D R N R I A A A E N N G N E S G V
 AGA GAG CTA AAA AGG ATT GTG CAG AAA GAA AAC TGG TTC TCT GCA TTT CTG AAT GTT
 R E L L K R I V Q K E N W F S A F L N V
 CTT CGT CAA ACA GGA AAC AAT GAA CTT GTC CAA GAG TTA ACA GGC TCT GAT TGC TCA GAA
 L R Q T G N N E L V Q E L T G S D C S E
 AGC AAT GCA GAG ATT GAG AAT TTA TCA CAA GTT GAT GGT CCT CAA GTG GAA GAG CAA CTT
 S N A E I E N L S Q V D G P Q V E E Q L

FIGURE 1A-2

CTT TCA ACC ACA GTT CAG CCA AAT CTG GAG AAG GAG GTC TGG GGC ATG GAG AAT AAC TCA
 L S T T V Q P N L E K E V W G M E N S
 TCA GAA TCA TCT TTT GCA GAT TCT TCT GTA GTT TCA GAA TCA GAC ACA AGT TTG GCA GAA
 S E S S F A D S S S V V S E S D T S L A E
 GGA AGT GTC AGC TGC TTA GAT GAA AGT CTT GGA CAT AAC AGC AAC ATG GGC AGT GAT TCA
 G S V S C L D E S L G H N S N M G S D S
 GGC ACC ATG GGA AGT GAT TCA GAT GAA GAG AAT GTG GCA GCA AGA GCA TCC CCG GAG CCA
 G T M G S D S D TAC CAA ATG GAA GTT GCC CAG CCA GCC TTG GAA GGG AAG AAT
 GAA CTC CAG CTC AGG CCT TAC CAA ATG GAA GTT GCC CAG CCA GCC TTG GAA GGG AAG AAT
 E L Q L R P Y Q M E V A Q P A L E G K N
 ATC ATC ATC TGC CTC CCT ACA GGG AGT GGA AAA ACC AGA GTG GCT GTT TAC ATT GCC AAG
 I I I C L P T G S G K T R V A V Y I A K
 GAT CAC TTA GAC AAG AAG AAA AAA GCA TCT GAG CCT GGA AAA GTT ATA GTT CTT GTC AAT
 D H L D K K K K A S E P G K V I V L V N
 AAG GTA CTG CTA GTT GAA CAG CTC TTC CGC AAG GAG TTC CAA CCA TTT TTG AAG AAA TGG
 K V L L V E Q L F R K E F Q P F L K K W
 TAT CGT GTT ATT GGA TTA AGT GGT GAT ACC CAA CTG AAA ATA TCA TTT CCA GAA GTT GTC
 Y R V I G L S G D T Q L K I S F P E V V
 AAG TCC TGT GAT ATT ATT ATC AGT ACA GCT CAA ATC CTT GAA AAC TCC CTC TTA AAC TTG
 K S C D I I I S T A Q I L E N S L L N L
 GAA AAT GGA GAA GAT GCT GGT GTT CAA TTG TCA GAC TTT TCC CTC ATT ATC ATT GAT GAA
 E N G E D A G V Q L S D F S L I I D E
 TGT CAT CAC ACC AAC AAA GAA GCA GTG TAT AAT AAC ATC ATG AGG CAT TAT TTG ATG CAG
 C H H T N K E A V Y N N I M R H Y L M Q
 AAG TTG AAA AAC AAT AGA CTC AAG AAA GAA AAC CCA GTG ATT CCC CTT CCT CAG ATA
 K L K N N R L K K E N K P V I P L P Q I
 CTG GGA CTA ACA GCT TCA CCT GGT GAT GGA GGG GCC ACG AAG CAA GCC AAA GCT GAA GAA
 L G L T A S P G V G G A T K Q A K A E E

FIGURE 1A-3

CAC ATT TTA AAA CTA TGT GCC AAT CTT GAT GCA TTT ACT ATT AAA ACT GTT AAA GAA AAC
H I L K L C A N L L D A F T I K T V K E M
CTT GAT CAA CTG AAA AAC CAA ATA CAG GAG CCA TGC AAG AAG TTT GCC ATT GCA GAT GCA
L D Q L K N Q I Q Q E P C K K F A I A D A
ACC AGA GAA GAT CCA TTT AAA GAG AAA CTT CTA GAA ATA ATG ACA AGG ATT CAA ACT TAT
T R E D P F K E K L L E I M T R I Q T Y
TGT CAA ATG AGT CCA ATG TCA GAT TTT GGA ACT CAA CCC TAT GAA CAA TGG GCC ATT CAA
C Q M S P M H S D F G T Q P Y E Q W A I Q
ATG GAA AAA GCT GCA AAA AAA GGA AAT CGC AAA GAA CGT GTT TGT GCA GAA CAT TTG
M E K K A A K K G N R K E R V C A E H L
AGG AAG TAC AAT GAG GCC CTA CAA AAT AAT GAC ACA ATT CGA ATG ATA GAT GCG TAT ACT
R K Y N E A L Q I N D T I R M I D A Y T
CAT CTT GAA ACT TTC TAT AAT GAA GAG AAA GAT AAG AAG TTT GCA GTC ATA GAA GAT GAT
H L E T F Y N E E K D G D K K F A V I E D D
AGT GAT GAG GGT GGT GAT GAT GAT GAT TGT GAT GGT GAT GAA GAT GAT GAT TTA AAG
S D E G G D D E Y C D G D E D E D D L K
AAA CCT TTG AAA CTG GAT GAA ACA GAT AGA TTT CTC ATG ACT TTA TTT TTT GAA AAC AAT
K P L K L D E T D R F L M T L F F E M N
AAA ATG TTG AAA AGG CTG GCT GAA AAC CCA GAA TAT GAA AAT GAA AAG CTG ACC AAA TTA
K M L K R L A E N P E Y E N E GCA CGA ATA ATC TTT
AGA AAT ACC ATA ATG GAG CAA TAT ACT AGG ACT GAG GAA TCA GCA GGA ATA ATC TTT
R N T I M E Q Y T R T E E S A R G I I F
ACA AAA ACA CAG AGT GCA TAT GCG CTT TCC CAG TGG ATT ACT GAA AAT GAA AAA TTT
T K T R Q S A Y A L S Q W I T E M E K F
GCT GAA GTA GGA GTC AAA GCC CAC CAT CTG ATT GGA GCT GGA CAC AGC AGT GAG TTC AAA
A E V G V K A H L I G A G H S S E F K

FIGURE 1A-4

CCC ATG ACA CAG AAT GAA CAA AAA GAA GTC ATT AGT AAA TTT CGC ACT GGA AAA ATC AAT
 P M T Q N E Q K E V I S K K F R T G K I M
 CTG CTT ATC GCT ACC ACA GTG GCA GAA GGT CTG GAT ATT AAA GAA TGT AAC ATT GTT
 L I A T V A E E G L D I K E C N I V
 ATC CGT TAT GGT CTC GTC ACC AAT GAA ATA GCC ATG GTC CAG GCC CGT GGT CGA GCC AGA
 I R Y G L V T N E I A M V Q A R A R
 GCT GAT GAG AGC ACC TAC GTC GTC CTG GTC GAT GGT TCA GGA GTT ATC GAA CAT GAG
 A D E S T Y V L V A H S G S G V I E H E
 ACA GTT AAT GAT TTC CGA GAG AAG ATG ATG TAT AAA GCT ATA CAT TGT GGT CAA AAT ATG
 T V N D F R E K M Y K A I H C V Q N M
 AAA CCA GAG GAG TAT GCT CAT AAG ATT TTG GAA TTA CAG ATG CAA AGT ATA ATG GAA AAG
 K P E Y A H K I L E L Q M Q S I M E K
 AAA ATG AAA ACC AAG AGA AAT ATT GCC AAG CAT TAC AAG AAT AAC CCA TCA CTA ATA ACT
 K M K T K R N I A K H Y K N N P S L I T
 TTC CTT TGC AAA AAC TGC AGT GTG CTA GCC TGT TCT GGG GAA GAT ATC CAT GTA ATT GAG
 F L C K N C S V L A C S G E D I H V I E
 AAA ATG CAT CAC GTC AAT ATG ACC CCA GAA TTC AAG GAA CTT TAC ATT GTA AGA GAA AAC
 K N H H V N M T P E F K E L Y I V R E N
 AAA GCA CTG CAA AAG AAG TGT GCC GAC TAT CAA ATA AAT GGT GAA ATC ATC TGC AAA TGT
 K A L Q K K C A D Y Q I N G E I I C K C
 GGC CAG GCT TGG GGA ACA ATG ATG GTG CAC AAA GGC TTA GAT TTG CCT TGT CTC AAA ATA
 G Q A W G T M M V H K G L D L P C L K I
 AGG AAT TTT GTA GTG GTT TTC AAA AAT AAT TCA ACA AAG AAA CAA TAC AAA AAG TGG GTA
 R N F V V V F K N N S T K Q Y K K W V
 GAA TTA CCT ATC ACA TTT CCC AAT CTT GAC TAT TCA GAA TGC TGT TTA TTT AGT GAT GAG
 E L P I T F P N L D Y S E C C L F S D E
 GAT TAG CAC TTG ATT GAA GAT TCT TTT AAA ATA CTA TCA GTT AAA CAT TTA ATA TGA TTA
 D *
 TGA TTA ATG TAT TCA TTA TGC TAC AGA ACT GAC ATA AGA ATC AAT AAA ATG ATT GTT TTA
 CTC TG

FIGURE 1B

CATTGAACTC	TTTTTAAGAA	CACAATATAT	TANGCATTAT	CCATCTTATT
GTTGGGCAGA	GGTAAGGAAA	ATNTACCAAT	AATTTTCATT	AGTGTGGAGC
ATTATANTCC	TGTGGAAAAGA	ATGCTGAAGT	ACAAATGAGA	ATCCAAAGTA
CCAGTCTCAG	TTCTGTCACT	AATTTTCAGA	ATAAAATTAG	GCAAATCAGT
TC				

FIGURE 1C

ICH-2

ICE

IAP1-453

IAP2-439

ICH-1

mda5-125

RAIDD

```

-MABGNHRKKPLKVLESGLGKDFLTGVLDNLVEQNVLNWKKEEKKYYD-AKTEDKVRVMA 58
-MADKVLKEKRKLFIKSMGEGTINGLLDELLQTRVLNKEEKKVREN-ATVMDKTRALI 58
MASDDLIRKNRMALFQQLTCVLPILDNLKANVINKEQHDIIKQK--TQIPLOARELI 58
-ESNDLLLIRKNRMALFQHLTCVIPILDSLLTAGIINEQEHDIKQK--TQTSLOARELI 57
-MHPPHQETLKKNRVVLAKQLLSELLEHLEKDIITLEMRELIQAK--VGSFSQNVELL 57
-----LVDKLLVRDVLDKCMEELLTIEDNRNRIAAENNGNESGVRELL 44
MEARDKQVLRSLRLELGAELVEGLVLYQEGILTENHIQIINAQ--TTGLRKTMLLL 58
: * : : * :

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ICH-2

ICE

IAP1-453

IAP2-439

ICH-1

mda5-125

RAIDD

```

DSMQEKQRMAGQMLLQTFNIDQISP-----NKKAHPNMEAGPPESGESTDALKLCPHE 112
DSVIPKGAQACQICITYICEEDSYLAGTLGLSAAPQAVQDNPAAMPTSSGSEGNVKLCSLE 118
DTLLVKGNAANIFKNCLKEIDSTLY-----KNLFVDKNMKYIP-----TEDVSGLSLEE 108
DTLLVKGNIATVFRNSLOEAEAVLY-----EHLFVQQDIKYIP-----TEDVSDLPVEE 107
NLLPKRGPOAFDAFCEALRETKQGHLED--MLLTLSGLQHVLPPLSCDYDLSLPFPVCE 115
KRIVQK-----LKKAREEAMTDLP-----AGDRLTGIPSH 50
DILPSRGPKAFDTFLDSLQEFFPWREK-----LKKAREEAMTDLP-----AGDRLTGIPSH 109
: : :

```

FIGURE 1D-1

eIF4A1	-----MSAQDSRSRDNGP-----	14
p68RNAhelicase	-----MSGYSSDRDRGRDRGFAPRFGG-----	23
Mda-5	LLLSTLEKGVWHLGWTREFVEALRRTGSPLAARYMNPDLTDLPSFSPENAHDEYQLLLNL	120
	:... .*	
eIF4A1	-----DGME-----PEGVIESNWN--	28
p68RNAhelicase	-----SRAGPLSGKKFGNP-----GEKLVKKKWNLD	49
Mda-5	LQPTLVDKLLVRDVLDKCMEEEELLTIEDRNRIAAAENNGNESGVRELLKRIVQKENWFS*	180
	. : !.:*	
eIF4A1	-----PKFEKNFYQEHHPDLARRTAQEVETYRRSKEITVRGH	87
p68RNAhelicase	EL-----FLNVLRTGNNELVQELTGSDCSESNAEIEIENLSQVDGPQVEEQLLSTTVQPNLEKEVWGM	240
Mda-5	-----EIVDSFDMMNLS-----ESLLRGIYAYG	51
eIF4A1	NCPKPVLFNFEANFP-----ANVMDVIARQN	113
p68RNAhelicase	ENNSSESSFADSSVVSSEDTSLAEGSVCLDESLGHNSNMGSDSGTMGSDSDENVAARA	300
Mda-5	. * : ..	
eIF4A1	FEKP-----SAIQQRATLPCIKGYDVIAQAQSGTGKTATFAISILQQIELD-----LKATQ	102
p68RNAhelicase	FTEP-----TAIQAQGWFPVALSGLDMVGVAQTGSGKTLSYLLPAIVHINHQPFLERGDGPI	169
Mda-5	SPEPELQRPYQMEVAQPALEGKNIICLPTGSGKTRVAVYIAKDHLDKK--KASEPGK	358
	:* . * . :..* :*:*** :::	
eIF4A1	ALVLAPTRELAAQQIQ-----	117
p68RNAhelicase	CLVLAPTRELAAQQVQ-----	184
Mda-5	VIVLVNKKVLLVEQLFRKEFPFLKKWYRVIGLSGDTQLKISFPEVVKSCDIIISTAQILE	418
	:**..*::*	

FIGURE 1D-2

EIF4A1	-----KVV 120
p68RNAhelicase	-----QVA 187
Mda-5	NSLLNLENGEDAGVQLSDFSLIIIDECHHTNKEAVYNNIMRHYLMQKLKNNRLKKNKPV 478
	:
EIF4A1	MALGDYMGASCHACIGGTNNVRAEVQKLQMEAPHIIIVGTPGRVFDMLNRRYLSPKYIKMFV 180
p68RNAhelicase	AEYCRACRLKSTCIYGGAPKGPQIRDLERG-VEICIAATPGRLLIDFLECGKTNLRRTTYLV 246
Mda-5	IPLPQILGLTASPGVGATKQAKAEHHILKLCANLDAFTIKTVKENLDQLKNQIQEPCKK 538
	**:
	.. : :
EIF4A1	LDEADEMLSRGFKDQIYDIFQKLNSNTQVVLLSATMPSDVLEVTKKFMRDPIRILVKKEE 240
p68RNAhelicase	LDEADRMIDMGFEFPQIRKIVDQIRPDQRTLMSATWPKEVRQLAEDFLKDYIHINIGALE 306
Mda-5	FAIADATREDPFKEKLEIMTRIQTQYCMSPMSDFGTQPYEQWAIQMEKKAACKGNRKER 598
	: ** . * : : . * : : . * : : . *
	: : : : : : : : : : :
EIF4A1	LTLEGIRQF-----YINVEREEWKLDTLCD--- 265
p68RNAhelicase	LSANHNILQ-----IVDVCHDVEKDEKLIR--- 331
Mda-5	VCAEHLRKYNEALQINDTIRMIDAYTHLETIFYNEEKDKKFAVIEDDSDEGGDDEYCDGDE 658
	: :
	: : : :
EIF4A1	-----LYETLTIT--- 273
p68RNAhelicase	-----LMEIIMSEKE- 341
Mda-5	DEDDLKKPLKLDETDRFLMTLFFENNMKLRLAENPEYENEKLTCLRNTIMEQYTRTEES 718
	:
	: *
EIF4A1	-QAVIFINTRR-----KVDWLTEKMHARDFTVSAMHGD-----MDQKRDVIMREF 318
p68RNAhelicase	NKTIVFVETKR-----RCDELTRKMRRDGWPAMGIHGD-----KSQQRDWVLNEF 387
Mda-5	ARGIIFTKRQSAYALSQWITENEKFAEVGVKAHHLIGAGHSSEFPKPMTQNEQEVISKF 778

FIGURE 1D-3

eIF4A1
p68RNAhelicase
Mda-5

```

RSGSSRVLLITTDLLARGIDVQVSLVINVDLPTNRENYTHRIGRG-----GRFGRKGV 371
KHGKAPILLIATDVASRGLDVEDVKFVINVDYPNSSEDIHRIGR-----ARSTKTGT 440
RTGKINLLIATTVAEGLDIKECNIVIRYGLVTNEIAMVQARGRARADESTYVLVAHSGS 838
: * . : ** : * : . : * : * : * : * : * : * : * : * : * : * : * :

```

eIF4A1
p68RNAhelicase
Mda-5

```

AINMVTEEDKRTRLRDIEIFYNTSIEEMPLNVADLI----- 406
AYTFFTPNNIKQVSDLISVLREANQAINPKLLQLVDRGSGRSRGRGGMKDDRRDRYSAG 500
GVIEHETVNDFFREKMMYKAHCVQNMKPEEYAHKILELQMQSIMKKMKTKRNIKHYKN 898
: . : . : . : . : . : . : . : . : . : . : . : . : . : . :

```

FIGURE 2A

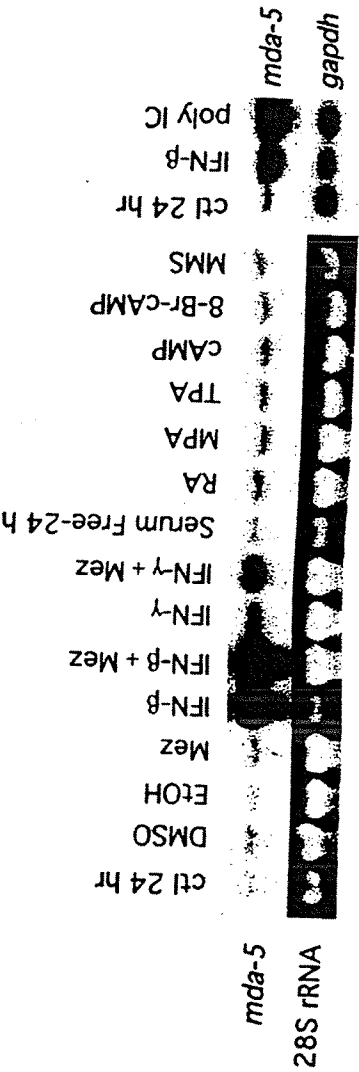


FIGURE 2B

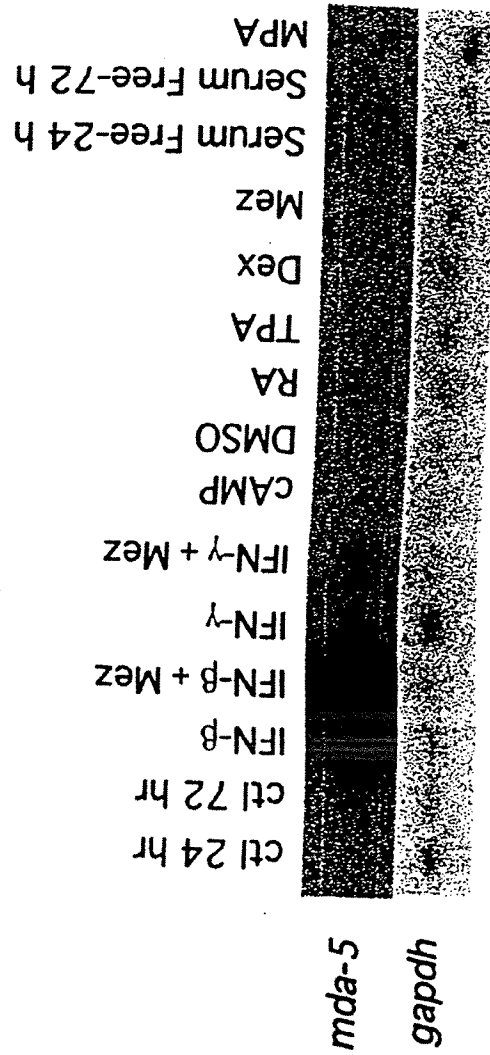


FIGURE 3A

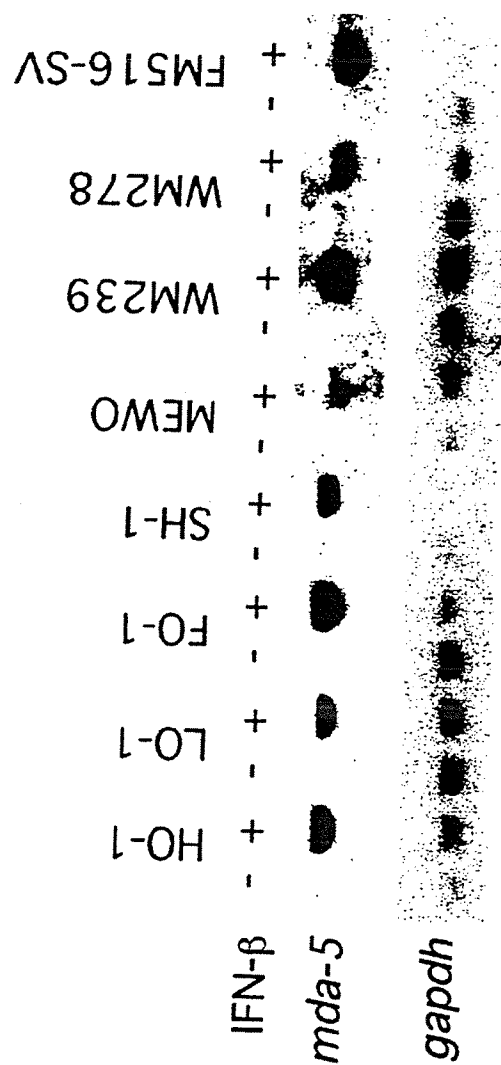


FIGURE 3B

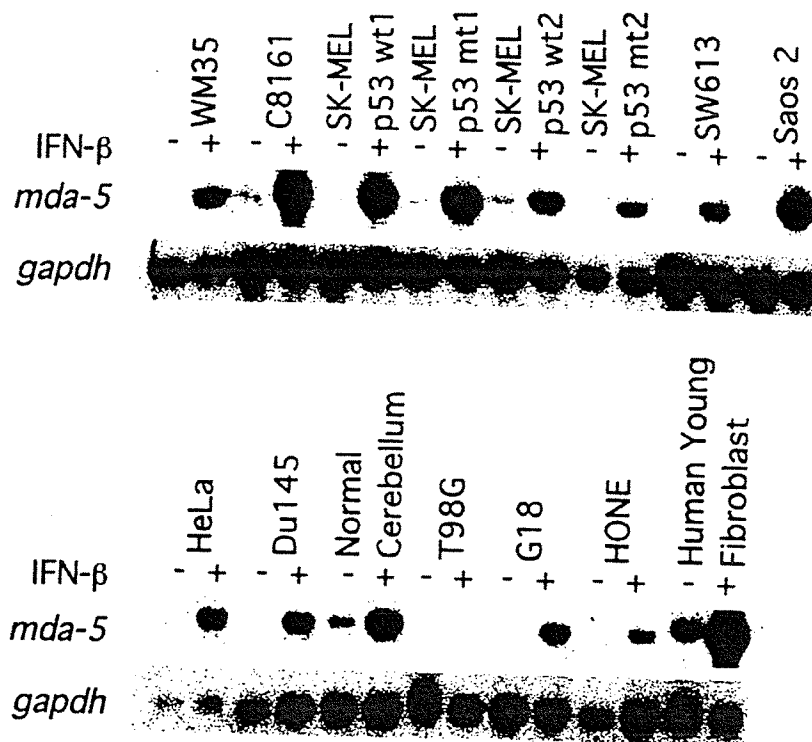


FIGURE 4A

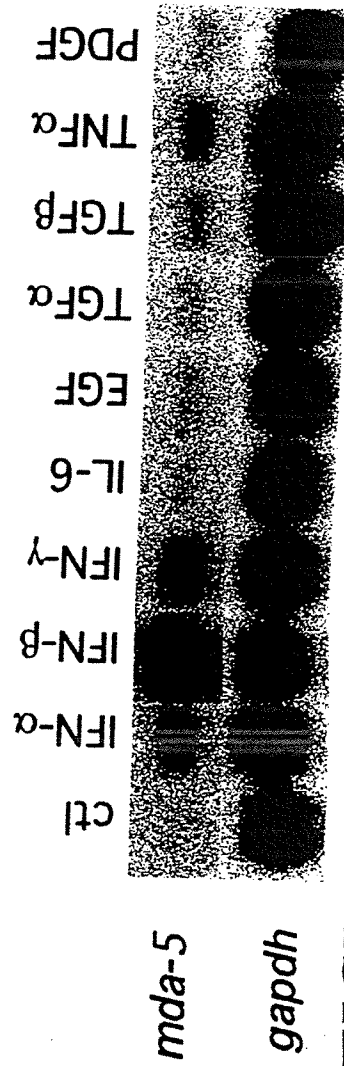


FIGURE 4B

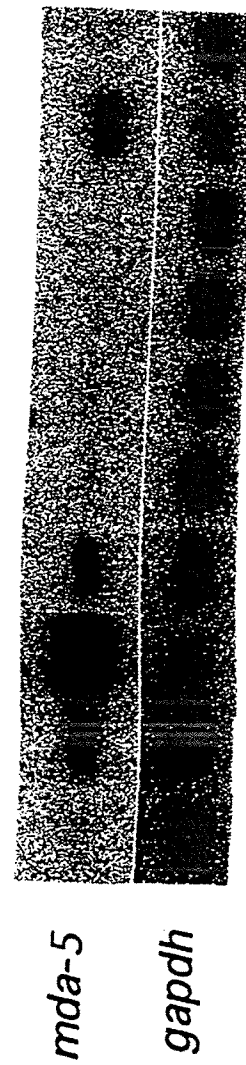


FIGURE 5

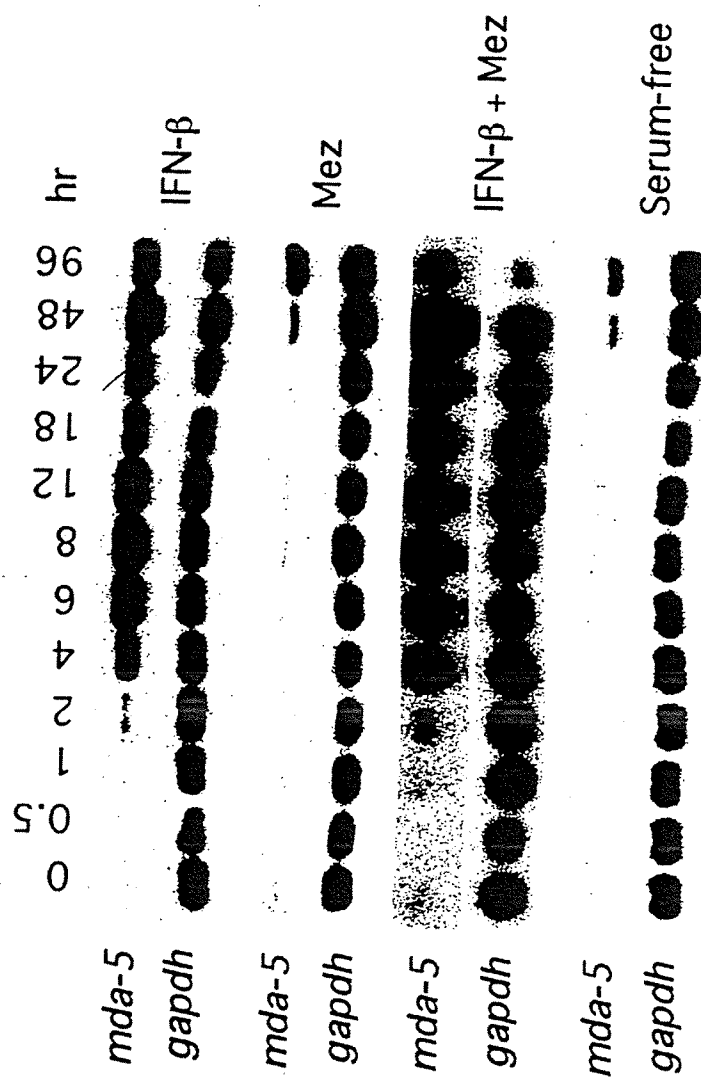


FIGURE 6

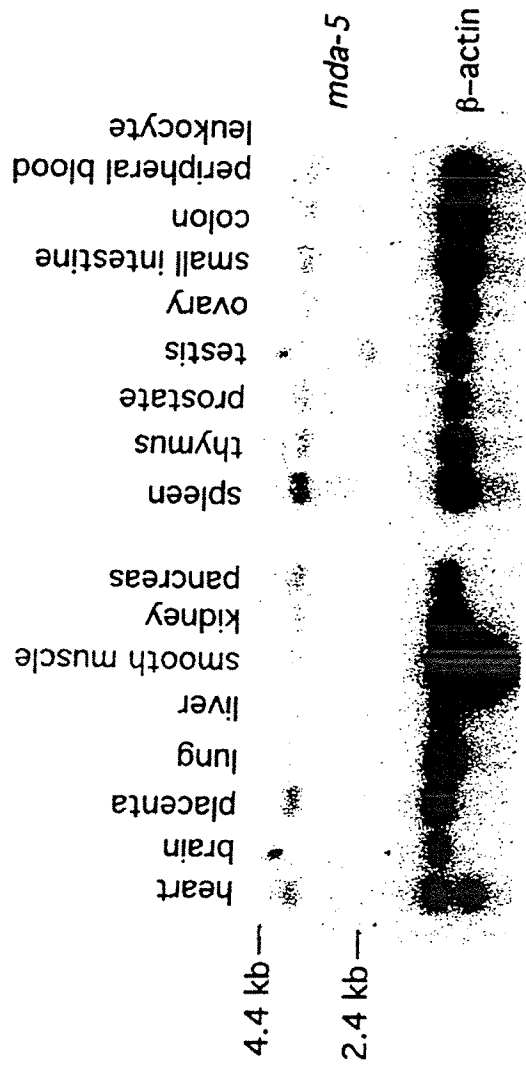


FIGURE 7A

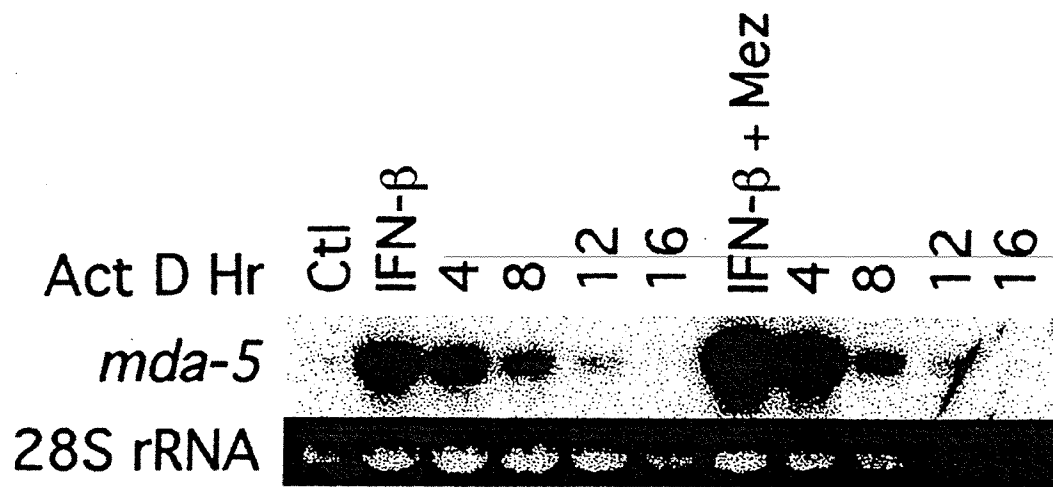


FIGURE 7B

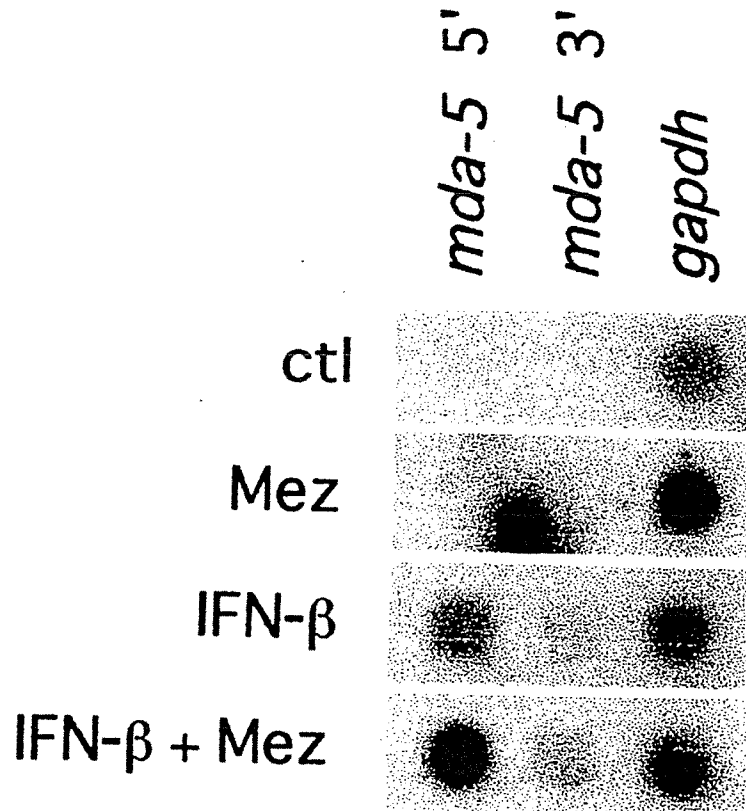


FIGURE 7C

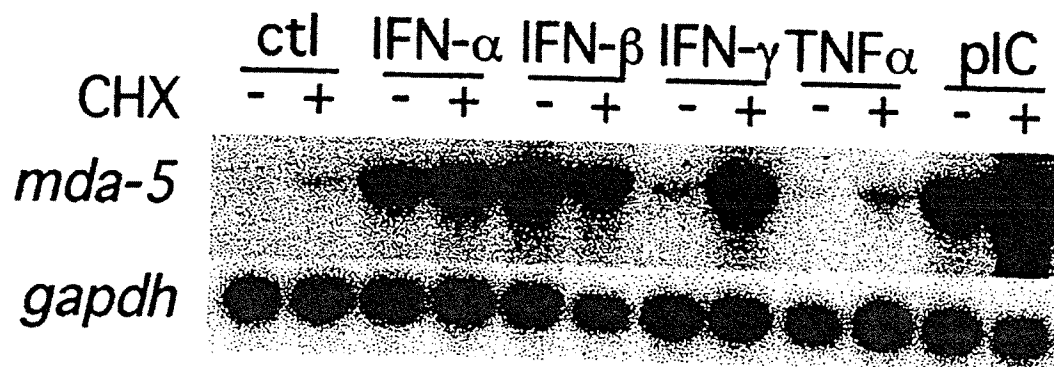


FIGURE 8A

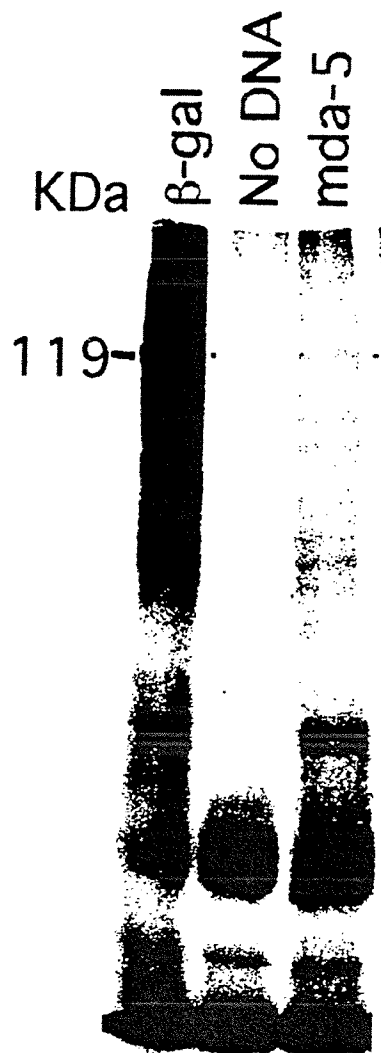


FIGURE 8B

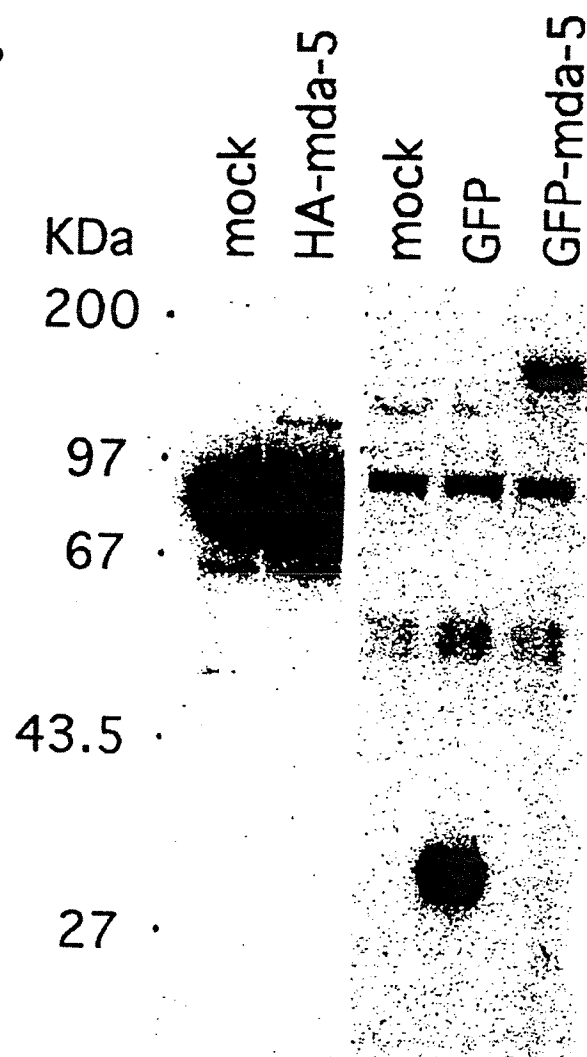
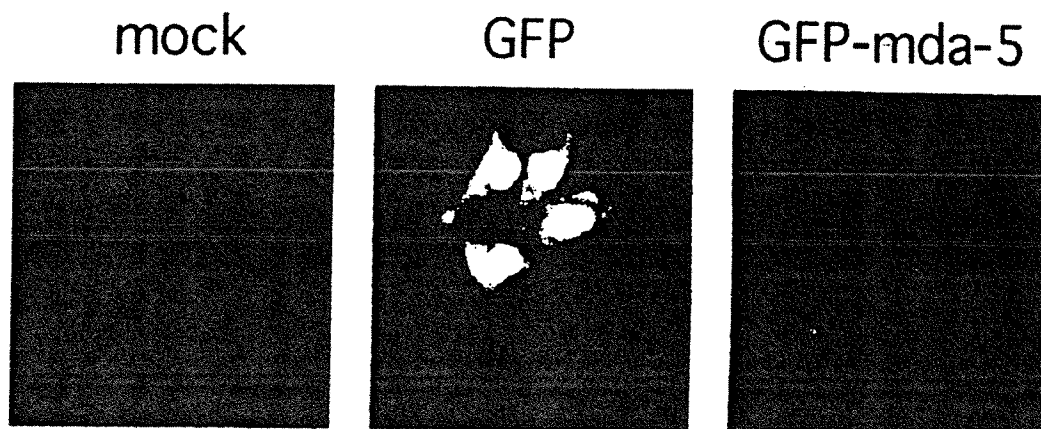
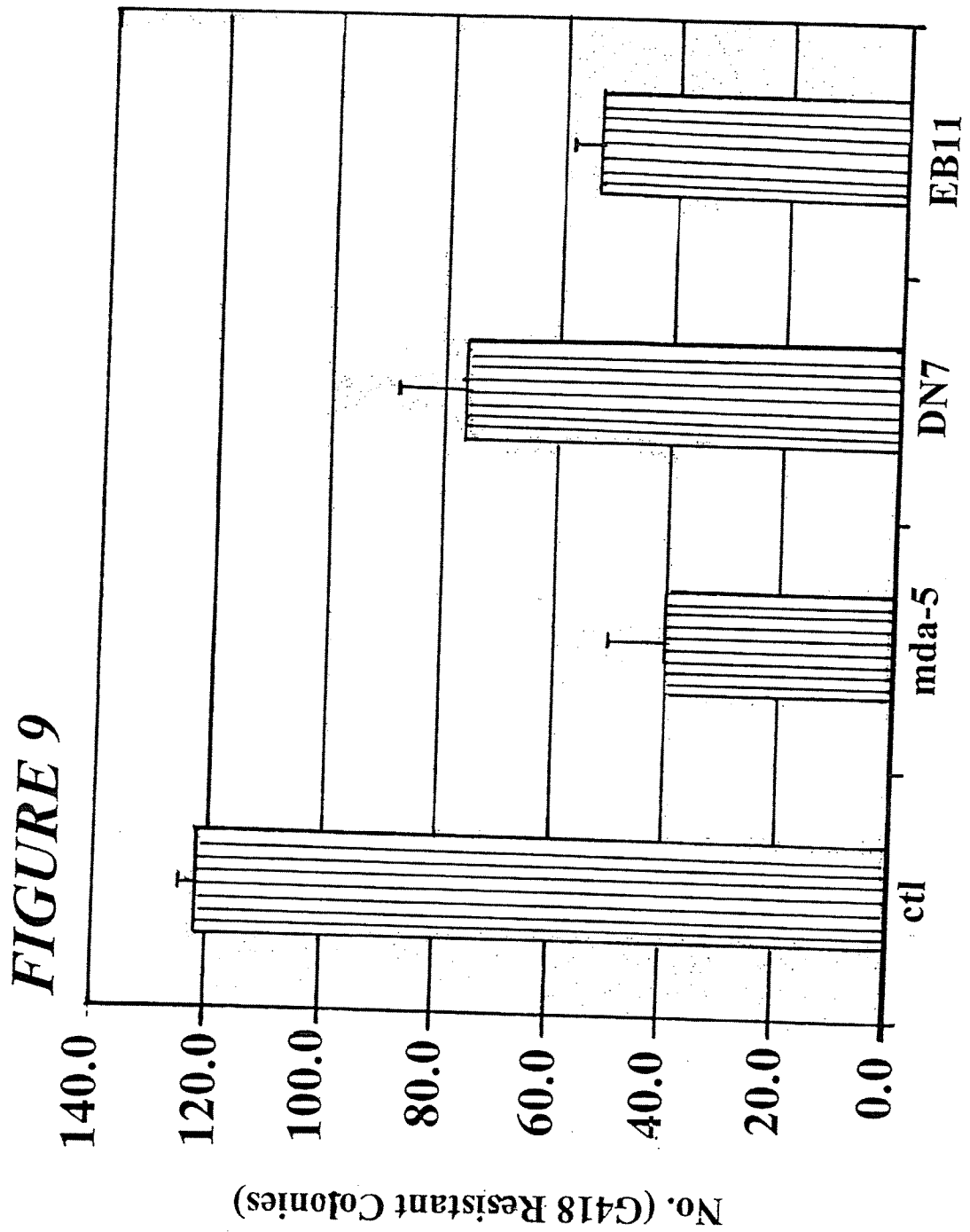


FIGURE 8C





REPLACEMENT DRAWING SHEET

FIGURE 10

GCACATTTTGGCCTACAAAGGACCTTATTGTTAAGGCAGAACCTGCTGGGAAAACAAAAT
 1 -----+-----+-----+-----+-----+-----+ 60

ECORI
 |
 ATCCGCCGGAGGAGCTTTGTAGAGCGTTGGTCTTGGTGTGAGAGAGAATTTCGCTTTCCTT
 61 -----+-----+-----+-----+-----+-----+ 120

TTCTGTTTCCCGCGGTGTCCTTAACCAAAGGCCTCCTCTCTTCACCCGCCCCGACCAAAA
 121 -----+-----+-----+-----+-----+-----+ 180

GGTGGCGTCTCCCTGAGGAACTCCCTCCCCGCCAGGCAGATTACGTTTACAAAGTCCTG
 181 -----+-----+-----+-----+-----+-----+ 240

AGAAGAGAATCGAAACAGAAACCAAAGTCAGGCAAACCTCTGTAAGAACTGCCTGACAGAA
 241 -----+-----+-----+-----+-----+-----+ 300

AGCTGGACTCAAAGCTCCTACCCGAGTGTGCAGCAGGATCGCCCCGGTCCGGGACCCAG
 301 -----+-----+-----+-----+-----+-----+ 360

GCGCACACCGCAGAGTCCAAAGTGCCGCGCCTGCCGGCCGCACCTGCCTGCCGCGGCCCC
 361 -----+-----+-----+-----+-----+-----+ 420

GCGCGCCGCCCCGCTGCCACCTGCCCGCCTGCCACCTGCCAGGTGCGAGTGCAGCCC
 421 -----+-----+-----+-----+-----+-----+ 480

CGCGCGCCGGCCTGAGAGCCCTGTGGACAACCTCGTCATTGTCAGGCACAGAGCGGTAGA
 481 -----+-----+-----+-----+-----+-----+ 540

CCCTGCTTCTNTAAGTGGGCAGCGGACAGCGGCACGCACATTTACCTGTCCCGCAGACA
 541 -----+-----+-----+-----+-----+-----+ 600

BstXI
 |
 ACAGCACCATCTGCTTGGGAGAACCCCTCTCCCTTCTCTGAGAAAGAAAGATGTCGAATGG
 601 -----+-----+-----+-----+-----+-----+ 660

GTATTCCACAGACGAGAATTTCCGCTATCTCATCTCGTGCTTCAGGGCCAGGGTGAAAAAT
 661 -----+-----+-----+-----+-----+-----+ 720

GTACATCCAGGTGGAGCCTGTGCTGGACTACCTGACCTTTCTGCCTGCAGAGGTGAAGGA
 721 -----+-----+-----+-----+-----+-----+ 780

GCAGATTCAGAGGACAGTCGCCACCTCCGGGAACATGCAGGCAGTTGAACTGCTGCTGAG
 781 -----+-----+-----+-----+-----+-----+ 840

ECORI
 |
 CACCTTGGAGAAGGGAGTCTGGCACCTTGGTTGGACTCGGGAATTTCGTGGAGGCCCTCCG
 841 -----+-----+-----+-----+-----+-----+ 900

SacI
 |
 GAGAACCGGCAGCCCTCTGGCCGCCCGCTACATGAACCCTGAGCTCACGGACTTGCCCTC
 901 -----+-----+-----+-----+-----+-----+ 960

TCCATCGTTTGAGAACGCTCATGATGAATATCTCCAACCTGCTGAACCTCCTTCAGCCAC
 961 -----+-----+-----+-----+-----+-----+ 1020

HindIII
 |
 BstXI
 |
 TCTGGTGGACAAGCTT
 1021 -----+-----+-----+-----+-----+ 1036

FIGURE 11A

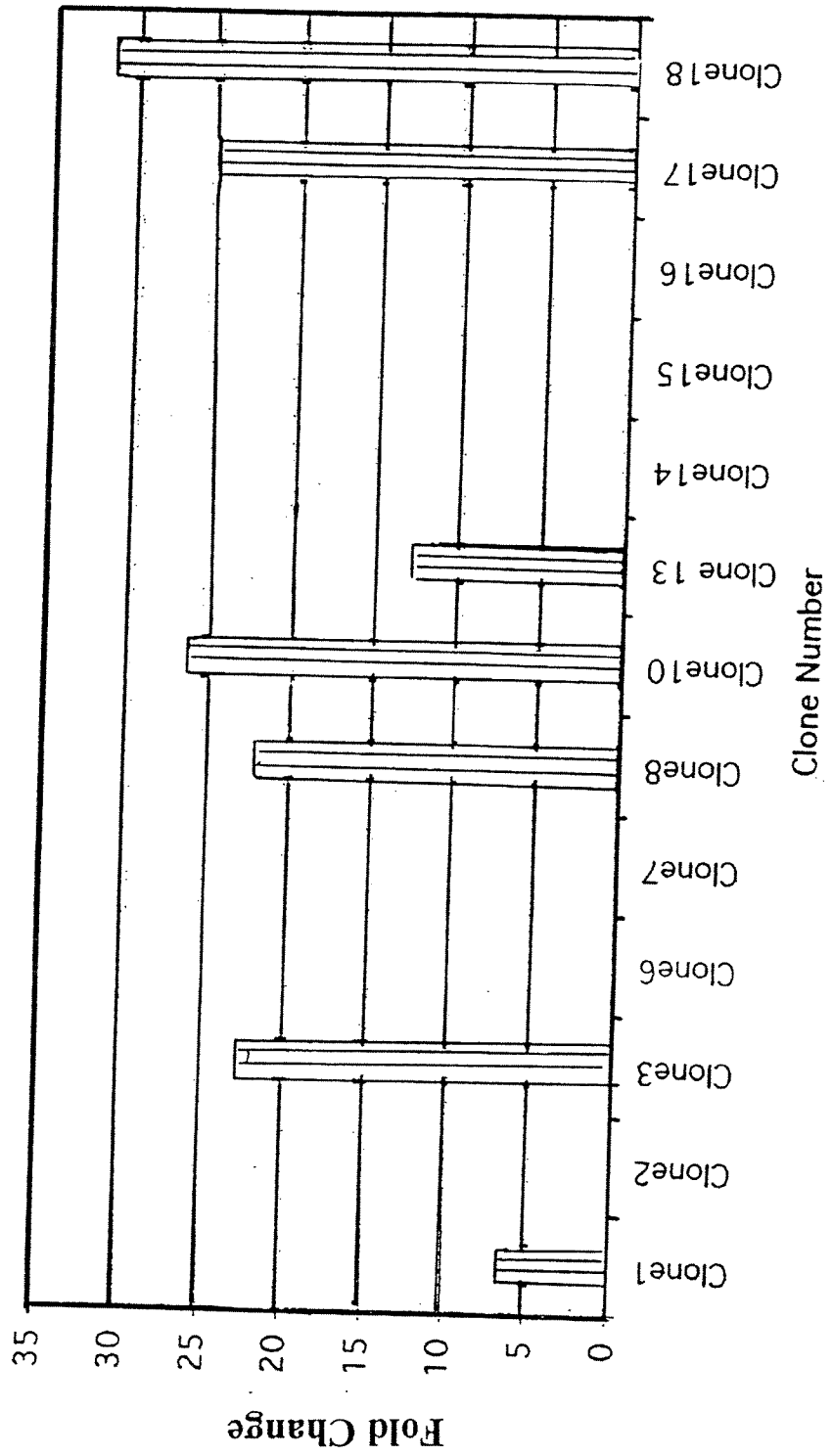


FIGURE 11B

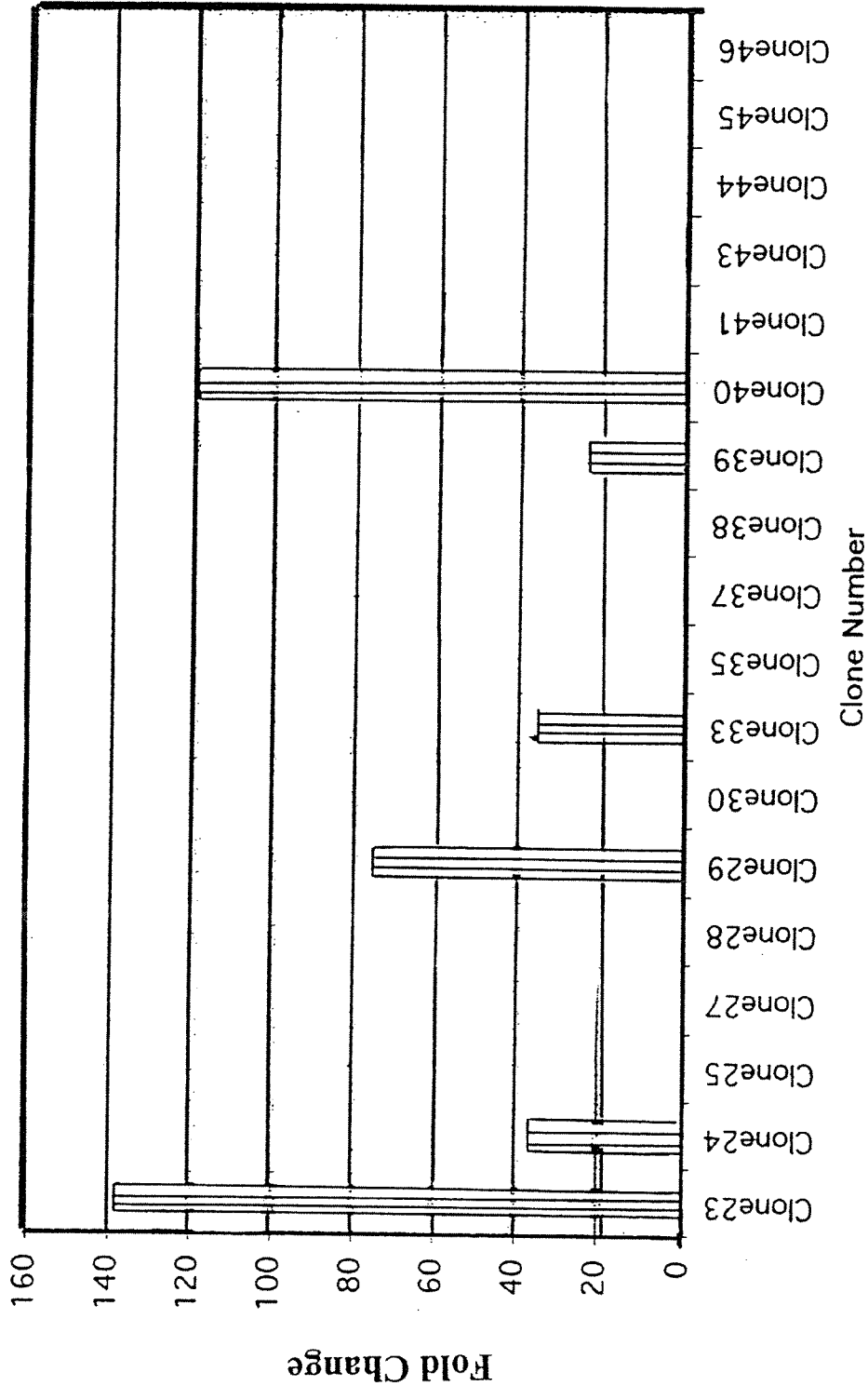


FIGURE 12A

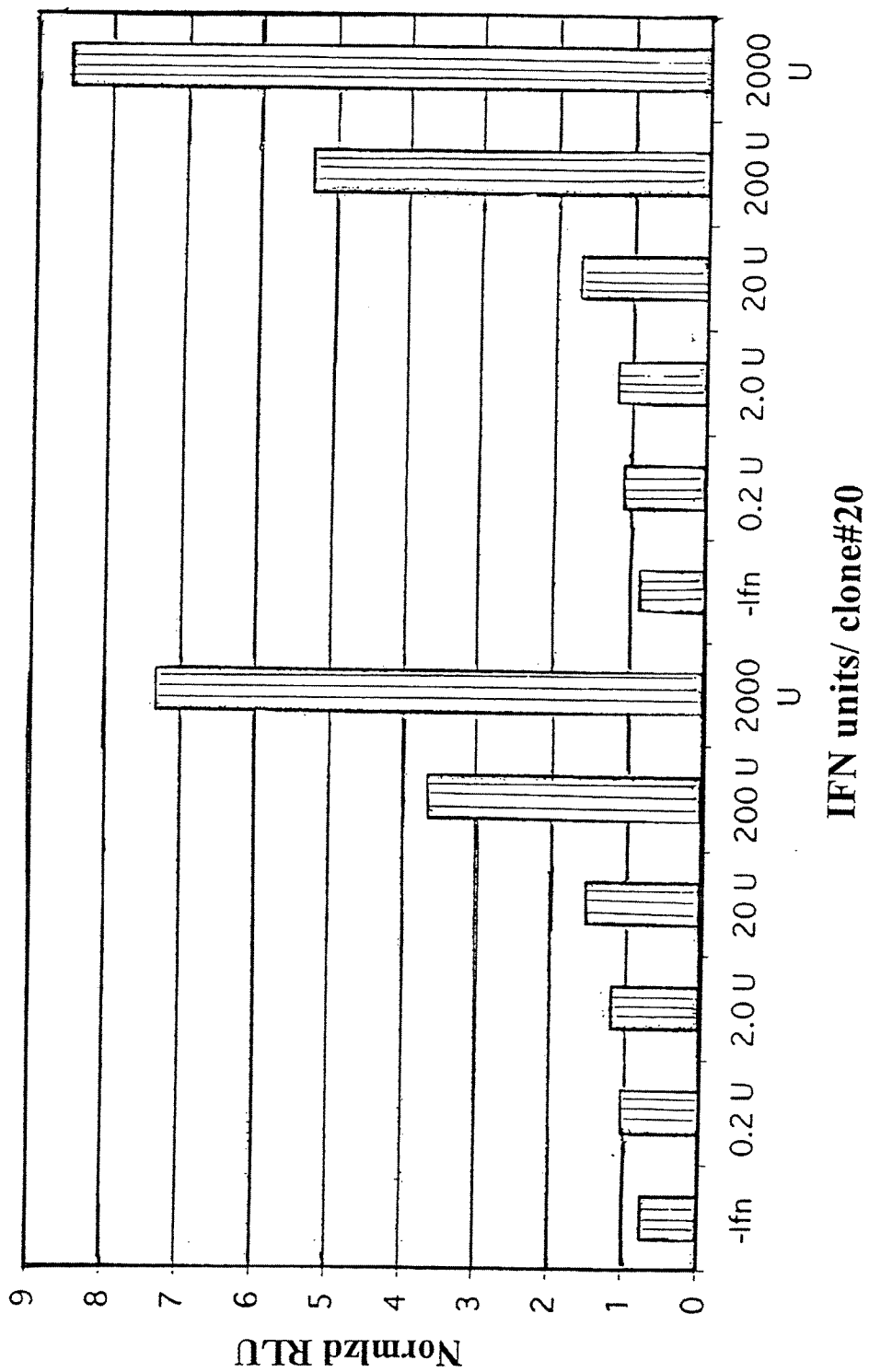


FIGURE 12B

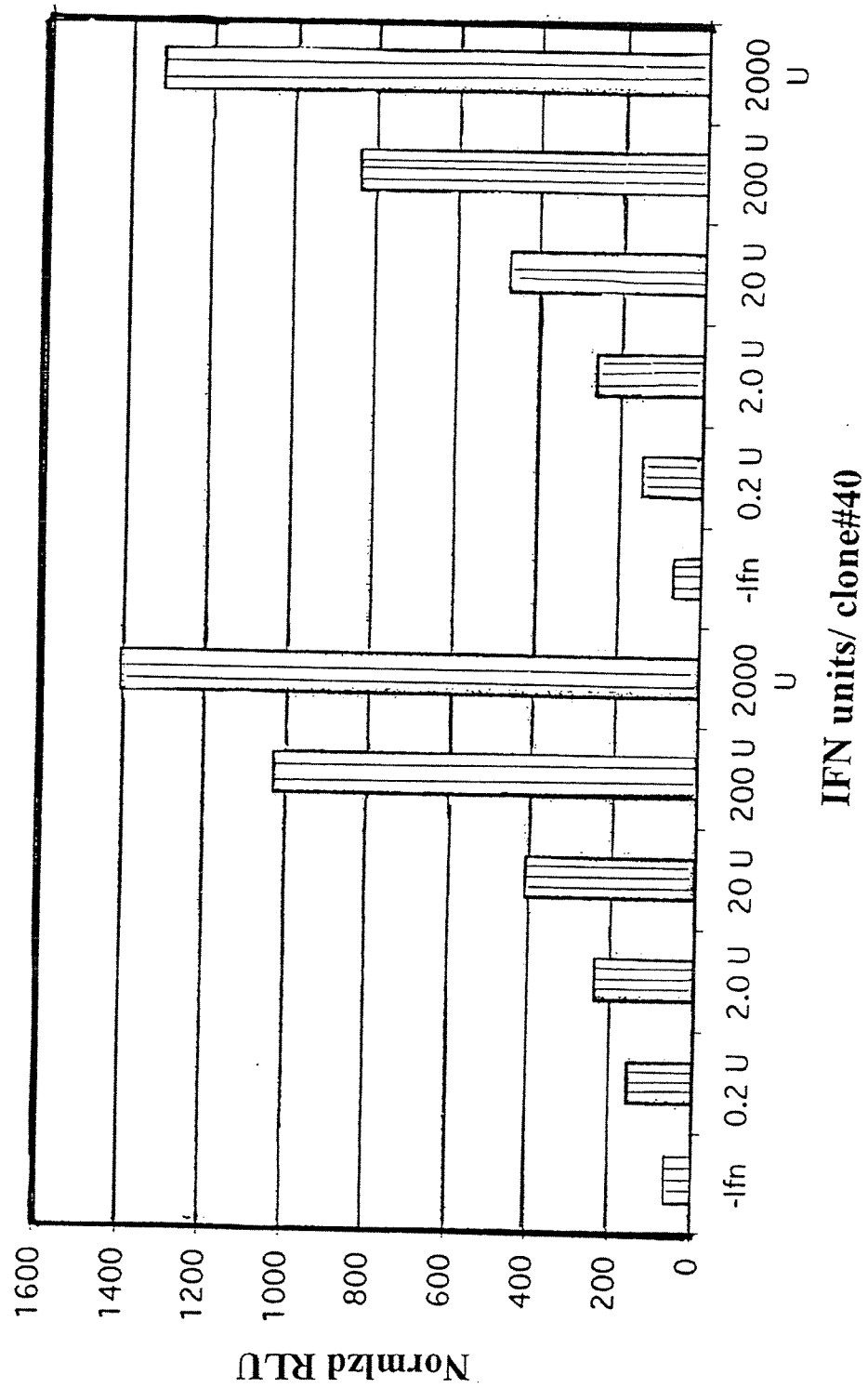


FIGURE 13A

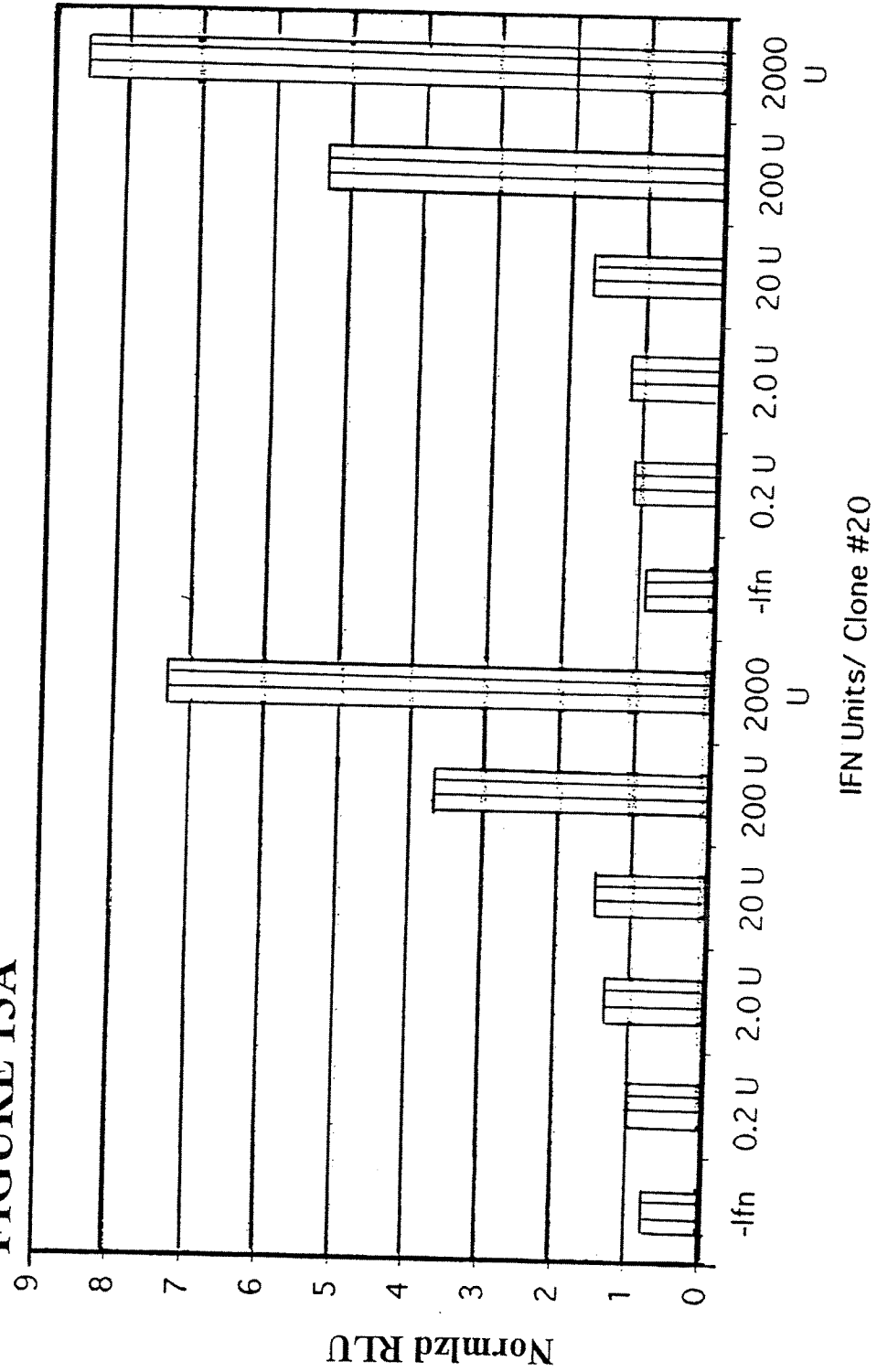


FIGURE 13B

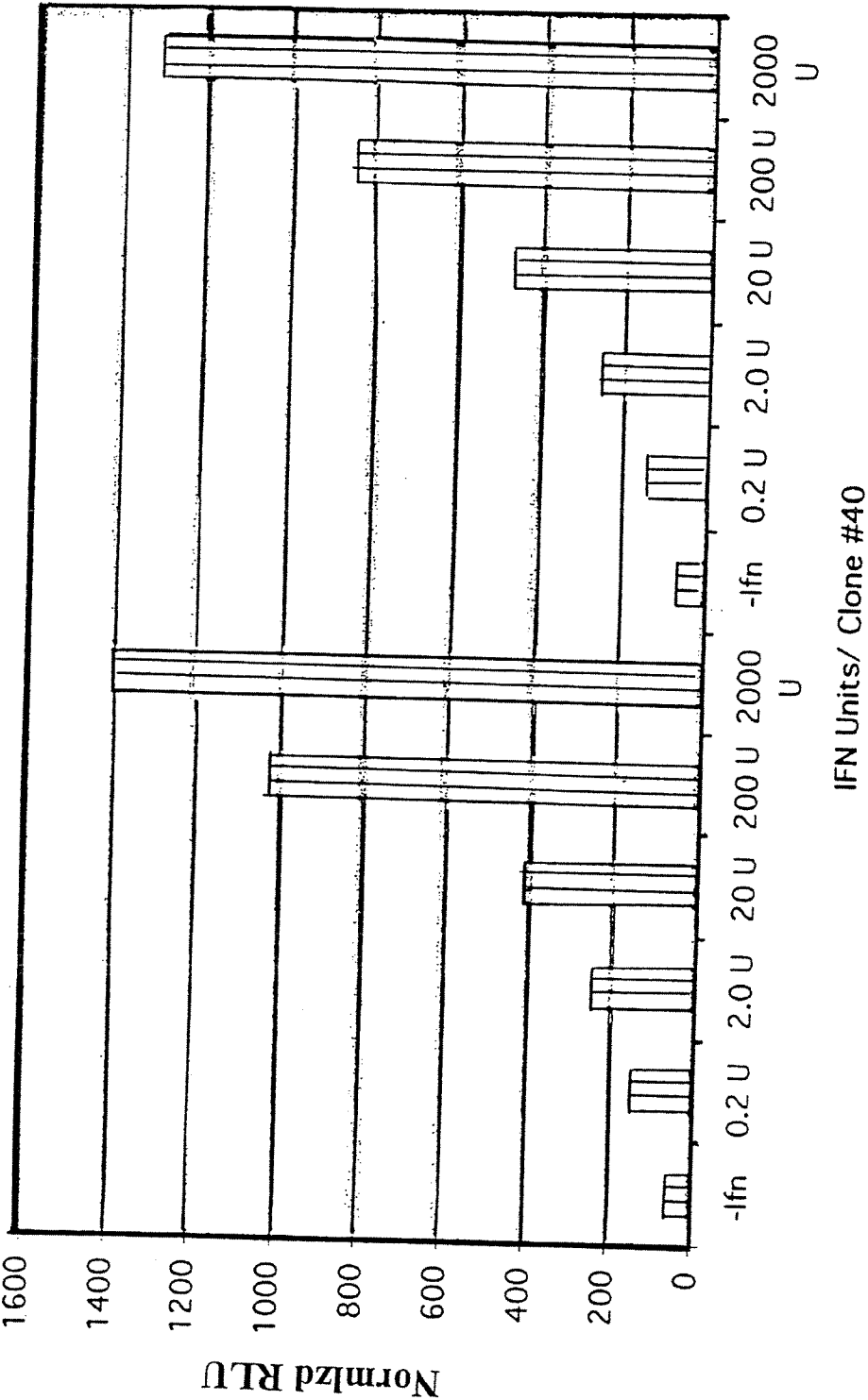


FIGURE 14A

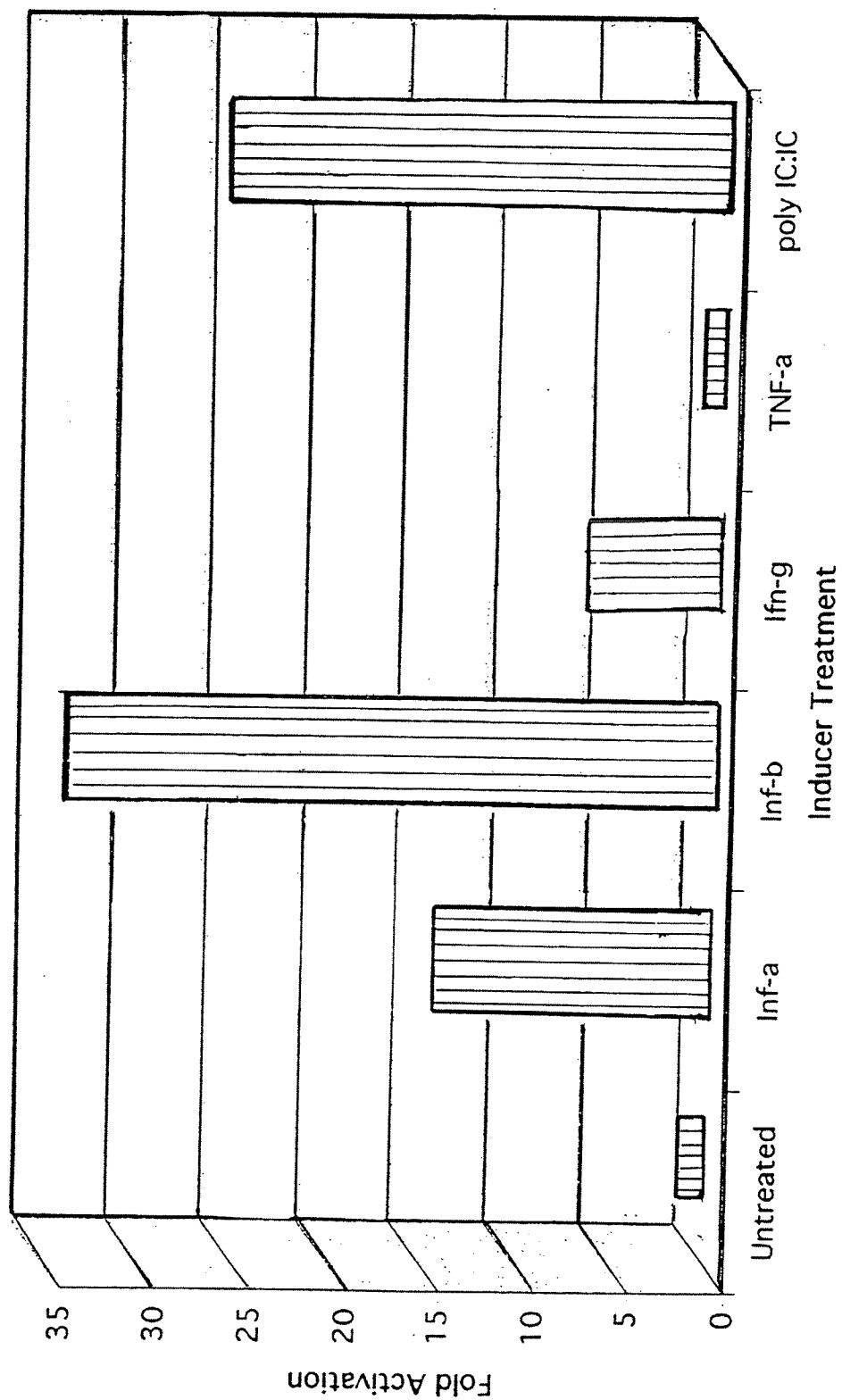


FIGURE 14B

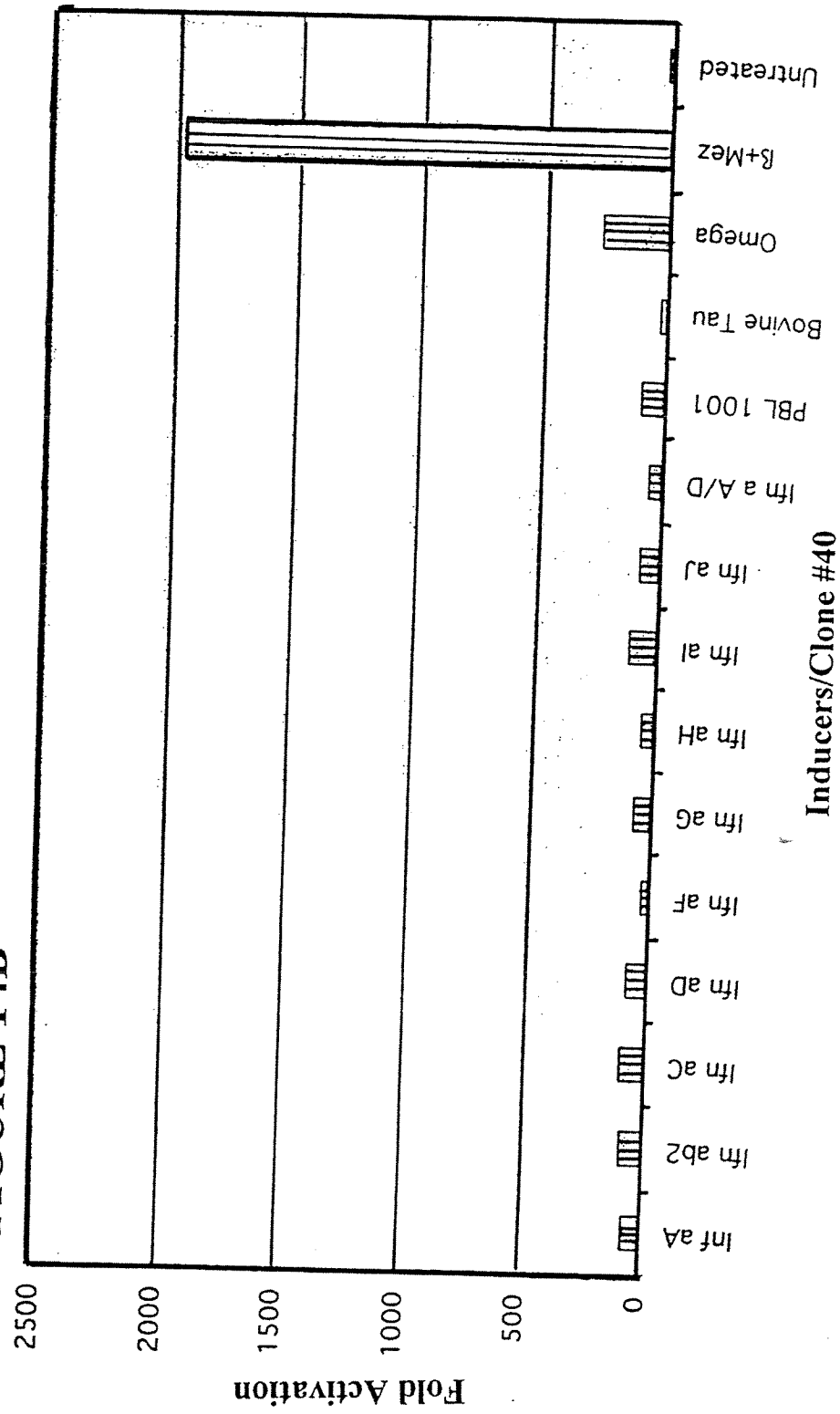


FIGURE 15A

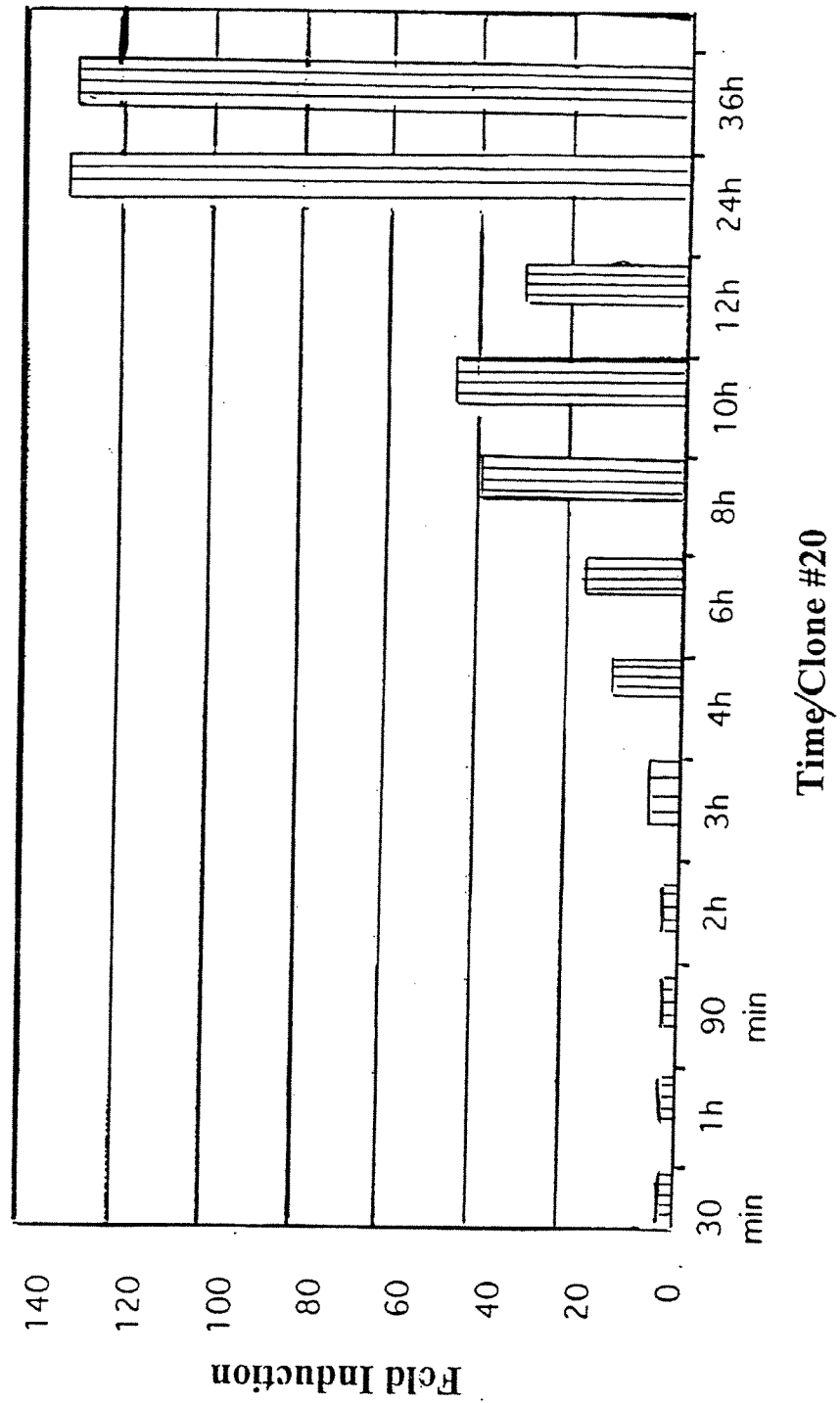


FIGURE 15B

